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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/480,236	01/10/2000	Mary Ellen Digan	4-31157A/USN	4092

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EXAMINER	
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ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/480,236	Applicant(s) Digan et al.
	Examiner G.R. Ewoldt	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *6/28/02 and 8/08/02* .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *35-54* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *35-54* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 35-54 are pending and being acted upon.

2. Applicant's corrected drawings and abstract are acknowledged. In view of Applicant's amendment and response, filed 8/08/02, in which all pending claims have been canceled, all previous rejections have been withdrawn. Note that where relevant to a new claim, Applicant's arguments have been addressed.

3. The following are new grounds for rejection necessitated by Applicant's amendment, filed 8/08/02.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 51-53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention, for the reasons of record as set forth in the rejections of Claims 31-33 in Papers No. 9 and 17, mailed 6/19/01 and 3/28/02, respectively.

Applicant's arguments, filed 8/08/02, have been fully considered but are not found persuasive. Applicant argues that, "Applicants' specification does provide unambiguous sequence information regarding the variable region of UCHT-1. The last paragraph on page 20 of application specifies the variable region in great detail. Specifically, the variable region of UCHT-1 is taught as comprising "residue 3 to 112 (light chain) and 128 to 249 (heavy chain) of SEQ. ID. NO:1 herein." This is unambiguous sequence information." It remains the Examiner's position that this disclosure, while describing SEQ ID NO:1, provides an inadequate description of sequences that are at least 90% identical to the variable region of UCHT-1 or antibodies about 90% as effective as UCHT-1 for binding human CD3.

Applicant argues "Regarding the "identity" requirement of claim 51, contrary to what is stated in the Office Action, Applicant's specification does teach a specific method for determining sequence identity," (last paragraph of page 22). "Applicant's claim 51 now specifically recites that the percent identity is determined by use of the Bestfit program." And "Moreover, determining the binding affinity of a given antibody for CD3 relative to UCHT-1 is well within the skill in the art, see, for example, the competitive FACS assay for binding in the article by J.M. Hexham et al., Molecular Immunology, 38, 397-408, 2001, included herewith. From the information available in the art and the teachings in the specification, it is submitted that one skilled in the art would have no problem determining those monoclonal antibodies that are about 90% as effective as UCHT-1 for binding human CD3." It is the Examiner's position that the specification provides one skilled in the art no more than a method by which said skilled artisan might test any particular antibody to see if it might be encompassed by the instant claims, i.e., the specification provides only a method of trial-and-error. A method of trial-and-error is an insufficient substitute for an actual description of the claimed invention. Accordingly, it remains the Examiner's position that the specification insufficiently describes the antibodies encompassed by the instant claims.

Regarding Applicant's assertion that the specification does provide "tangible structural features", e.g., SEQ ID NO:2 and the variable region of UCHT-1, these are not necessarily "tangible structural features" of the claimed variants. Additionally, Applicant's newly claimed limitation that the hybridizing polynucleotide be at least 300 bases in length still comprises an inadequate description of the claimed invention.

6. Claims 50-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for,

a recombinant immunotoxin polypeptide consisting of the polypeptide encoded by the nucleotide sequence of SEQ ID NO:2, does not reasonably provide enablement for:

a recombinant immunotoxin polypeptide comprising an antibody having a variable region which is at least about 90% identical to the variable region of UCHT-1 and is at least about 90% as effective as UCHT-1 for binding human CD3, for the reasons of record as set forth in the rejections of Claims 31-33 in Paper No. 17, mailed 3/28/02.

Applicant's arguments, filed 8/08/02, have been fully considered but are not found persuasive. Applicant argues that, "Applicants have provided sufficient information in order for one to practice the invention as claimed." And "It is submitted that the scope and detail of Applicants' disclosure do fairly provide suitable procedures for obtaining the immunotoxins of the invention." Applicant's argument appears to be that while the work of establishing which antibodies would be encompassed by the claims might be labor-intensive, it is not undue experimentation. It is the Examiner's position that the specification provides only a method of trial-and-error, and that trial-and-error provides no particular expectation of success in determining whether or not any particular antibody meets the limitations of the claims, i.e., they are unpredictable. Accordingly, methods of trial-and-error are considered to require undue experimentation.

7. Claim 50 is rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, "the polypeptide encoded by the complement of a nucleotide sequence having at least 300 bases which hybridizes to the nucleotide sequence of Claim 49 (SEQ. ID. NO:2)."

Applicant's amendment, filed 8/08/02, asserts that no new matter has been added. Applicant has indicated that at page 38 support for the new limitation can be found. However, no support for the complement of a polynucleotide having at least 300 bases has been found on the page.

8. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 35-54 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 6,103,235 (2000, of record) in view of Kreitman et al. (1995, of record) and Kreitman et al. (1994, of record), for the reasons of record as set forth in the rejections of Claims 1-7, 9-16, 29-30, and 33-34, in Paper No. 17, mailed 3/28/02.

Applicant's arguments, filed 8/08/02, have been fully considered but are not found persuasive. Applicant argues that, "The Kreitman et al. paper compares the activities of several immunotoxins directed against Tac (not CD3 as presently claimed). The data in Table 34 [*sic*] of the reference show the ability of different patients [sic] blood cells to be killed by the different immunotoxins. There is no predictability or pattern to the results. That is, *a priori*, one could not predict the effectiveness of a given PE-Tac immunotoxin on a given cell population by knowing the activity of a given DT-Tac immunotoxin on that cell population." And "Thus, one skilled in the art having the prior art before him could not *a priori* reasonably predict the effectiveness for a particular use of an anti-CD3-PE based immunotoxin with the knowledge that an anti-CD3-DT based immunotoxin is effective for that use." It is the Examiner's position that true or not, Applicant's assertions are irrelevant. The instant claims are drawn to a product, i.e., an immunotoxin, not a method of using an immunotoxin. Accordingly, the references need only provide a motivation to make the immunotoxin of the instant claims. While it may be that the DT versus PE immunotoxins vary in cytotoxicity, by an order of magnitude in some instances, they all remain cytotoxic. Thus, in at least that aspect they are interchangeable. Applicant also asserts that the asserted variable cytotoxicity is unpredictable, if that is so, then the skilled artisan would have the additional motivation of preparing the immunotoxin of the instant claims to see if it possessed the sought after degree of cytotoxicity. Contrary to Applicant's assertion, predictability for any particular use need not be the motivation for preparing the product of the instant claims.

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805 The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
November 19, 2002

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